ROCESSING COMPLETED FOR L7
L8 4 DUP REM L7 (6 DUPLICATES REMOVED)

=> dis l8 1-4 ibib abs

L8 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:107538 CAPLUS
DOCUMENT NUMBER: 136:149862
TITLE: Modified human carcinoembryonic antigen CAP-1 peptides and their use in cancer vaccines
INVENTOR(S): Berinstein, Neil; Tartaglia, James; Tine, John A.; Panicali, Dennis L.; Gritz, Linda; **Schlom, Jeffrey**
PATENT ASSIGNEE(S): Aventis Pasteur Limited, Can.; Therion Biologics; National Cancer Institute
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002010379	A2	20020207	WO 2001-CA1092	20010727

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-222043P P 20000731
AB The invention discloses immunogenic **CEA** (carcinoembryonic antigen) **agonist** polypeptides/proteins comprising a modified **epitope** contg. the amino acid sequence YLSGADLNL, nucleic acids coding therefor, vectors and/or cells comprising said nucleic acids, and mixts. and/or compns. thereof. Methods for eliciting or inducing **CEA**-specific immune responses utilizing the aforementioned agents are also disclosed. Use of the modified **CEA** CAP-1 polypeptide and the nucleic acid sequence encoding it in the treatment of gastrointestinal, breast, pancreatic, ovarian, lung or prostate cancer is provided. Methods for generation of viral vectors encoding the said sequence are provided. These include poxviruses, adenoviruses and alphavirus components.

L8 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:803641 CAPLUS
DOCUMENT NUMBER: 136:323457
TITLE: Carcinoembryonic antigen as a vaccine target
AUTHOR(S): **Schlom, Jeffrey**; Tsang, Kwong Y.; Hodge, James W.; Greiner, John W.
CORPORATE SOURCE: Neth.
SOURCE: Immunology and Medicine Series (2001), 30(Cancer Immunology), 73-100
CODEN: IMSMCU
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review discussed human carcinoembryonic antigen (**CEA**) as a target for vaccine-mediated therapy of a range of human cancers. An overview of the **CEA** gene family and the levels of expression of **CEA** in neoplastic and preneoplastic lesions, and in some normal and fetal tissues, is provided. The pros and cons of using animal models are discussed for defining the optimal strategies to induce an immune response and an antitumor response to a "self"-antigen such as **CEA** . Several studies were carried out to define the immunogenicity of **CEA** in humans, including studies on the definition of an enhancer T-cell **agonist epitope** that was shown to enhance T-cell responses to **CEA**. There are multiple strategies that can be used to further enhance the immunogenicity of a self-antigen such as **CEA**, including the use of vectors contg. multiple transgenes of T-cell costimulatory mols. The potential for implementation of these strategies in vaccine clin. trials is also discussed.
REFERENCE COUNT: 96 THERE ARE 96 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 4 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2000175479 MEDLINE
DOCUMENT NUMBER: 20175479 PubMed ID: 10709104
TITLE: **Agonist** peptide from a cytotoxic t-lymphocyte **epitope** of human carcinoembryonic antigen stimulates production of tc1-type cytokines and increases tyrosine phosphorylation more efficiently than cognate peptide.
AUTHOR: Salazar E; **Zaremba S**; Arlen P M; Tsang K Y; **Schlom J**
CORPORATE SOURCE: Laboratory of Tumor Immunology and Biology, National Cancer Institute, National Institutes of Health, Bethesda, MD 20892-1750, USA.
SOURCE: INTERNATIONAL JOURNAL OF CANCER, (2000 Mar 15) 85 (6) 829-38.
Journal code: GQU; 0042124. ISSN: 0020-7136.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 20000330
Last Updated on STN: 20000330
Entered Medline: 20000323
AB The identification of an **agonist** peptide (YLSGADLNL, designated CAP1-6D) to an immunodominant cytotoxic T-lymphocyte (CTL) **epitope** (designated CAP1) of human carcinoembryonic antigen (**CEA**) has previously been reported. The **agonist** peptide harbors a single amino acid substitution at a non-MHC anchor residue and is proposed to exert its effects at the level of the T-cell receptor (TCR). The type and magnitude of cytokines produced by CAP1-reactive CTL upon stimulation with the ***agonist*** peptide, CAP1-6D, were compared to those obtained upon stimulation with the cognate CAP1 peptide. In addition, early events

in the TCR signaling pathway were examined for differences in tyrosine phosphorylation. Upon stimulation with the **agonist** peptide CAP1-6D, several different **CEA**-specific CTL lines exhibited a marked shift in the peptide dose response, which resulted in as much as a 1,000-fold increase in the levels of GM-CSF and gamma-IFN produced as compared with the use of the CAP1 peptide. However, levels of IL-4 and IL-10, which are associated with anti-inflammatory effects, were very low or non-existent. The cytokine profile of CAP1- and CAP1-6D-specific CTL is consistent with a Tc1-type CTL. Consistent with these findings, **CEA**-specific CTL showed increased tyrosine phosphorylation of TCR signaling proteins ZAP-70 and TCR zeta chains in response to both peptides. However, when CAP1-6D was compared with the wild-type peptide, the increase in ZAP-70 phosphorylation was greater than the increase in zeta phosphorylation. CTL generated with the CAP1-6D **agonist** were shown capable of lysis of human carcinoma cells expressing native **CEA**. The ability to upregulate the production of GM-CSF, gamma-IFN, TNFalpha and IL-2 with the **agonist** peptide, as compared with CAP1, may help in initiating or sustaining anti-tumor immune responses and thus potentially prove to be useful in the treatment of **CEA**-positive tumors.

L8 ANSWER 4 OF 4 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 1998021980 MEDLINE
DOCUMENT NUMBER: 98021980 PubMed ID: 9377571
TITLE: Identification of an enhancer **agonist** cytotoxic T lymphocyte peptide from human carcinoembryonic antigen.
AUTHOR: **Zaremba S**; **Barzaga E**; Zhu M; Soares N; Tsang K Y; **Schlom J**
CORPORATE SOURCE: Laboratory of Tumor Immunology and Biology, Division of Basic Sciences, National Cancer Institute, Bethesda, Maryland 20892-1750, USA.
SOURCE: CANCER RESEARCH, (1997 Oct 15) 57 (20) 4570-7. Journal code: CNF; 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199711
ENTRY DATE: Entered STN: 19971224
Last Updated on STN: 19971224
Entered Medline: 19971110

AB A vaccination strategy designed to enhance the immunogenicity of self-antigens that are overexpressed in tumor cells is to identify and slightly modify immunodominant **apitopas** that elicit T-cell responses. The resultant T cells, however, must maintain their ability to recognize the native configuration of the peptide-MHC interaction on the tumor cell target. We used a strategy to enhance the immunogenicity of a human CTL **apitope** directed against a human self-antigen, which involved the modification of individual amino acid residues predicted to interact with the T-cell receptor; this strategy, moreover, required no prior knowledge of these actual specific interactions. Single amino acid substitutions were introduced to the CAP1 peptide (YLSGANLNL), an immunogenic HLA-A2+-binding peptide derived from human carcinoembryonic antigen (**CEA**). In this study, four amino acid residues that were predicted to potentially interact with the T-cell receptor of CAP1-specific CTLs were systematically replaced. Analogues were tested for binding to HLA-A2 and for recognition by an established CTL line directed against CAP1. This line was obtained from peripheral blood mononuclear cells from an HLA-A2+ individual vaccinated with a vaccinia-**CEA** recombinant. An analogue peptide was identified that was capable of sensitizing CAP1-specific CTLs 10(2)-10(3) times more efficiently than the native CAP1 peptide. This enhanced recognition was shown not to be due to better binding to HLA-A2. Therefore, the analogue CAP1-6D (YLSGADLNL, Asn at position 6 replaced by Asp) meets the criteria of a CTL enhancer **agonist** peptide. Both the CAP1-6D and the native CAP1 peptide were compared for the ability to generate specific CTL lines in vitro from unimmunized apparently healthy HLA-A2+ donors. Whereas CAP1 failed to generate CTLs from normal peripheral blood mononuclear cells, the **agonist** peptide was able to generate CD8+ CTL lines that recognized both the **agonist** and the native CAP1 sequence. Most importantly, these CTLs were capable of lysing human tumor cells endogenously expressing **CEA**. The use of enhancer **agonist** CTL peptides may thus represent a new efficient direction for immunotherapy protocols.

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L14 3 L13 NOT L8

=> dis l14 ibib abs

L14 ANSWER 1 OF 3 MEDLINE
ACCESSION NUMBER: 2002219664 MEDLINE
DOCUMENT NUMBER: 21953247 PubMed ID: 11956282
TITLE: Carcinoembryonic antigen as a target for therapeutic anticancer vaccines: a review.
AUTHOR: Berinstein Neil L
CORPORATE SOURCE: Aventis Pasteur Ltd, Toronto, Ontario, Canada.. neil.berinstein@aventis.com
SOURCE: JOURNAL OF CLINICAL ONCOLOGY, (2002 Apr 15) 20 (8) 2197-207. Ref: 72
Journal code: 8309333. ISSN: 0732-183X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200204
ENTRY DATE: Entered STN: 20020417
Last Updated on STN: 20020501
Entered Medline: 20020430

AB PURPOSE: To describe the features of carcinoembryonic antigen (**CEA**) that are important for its use in vaccination approaches and review the clinical experience with therapeutic vaccines targeting **CEA**. METHODS: A PubMed search was performed on **CEA**, along with various qualifiers such as cancer vaccines, **epitopes**, and function. Relevant articles were reviewed. RESULTS: **CEA** is a member of the immunoglobulin supergene family and may play a role in tumorigenesis. **CEA** protein is processed and presented on major histocompatibility complex (MHC) proteins for multiple alleles, including HLA A2, A3, and A24. T lymphocytes from healthy volunteers and cancer patients can recognize the processed **epitopes** of **CEA** and can become activated to lyse **CEA**-expressing tumors. Therapeutic vaccination approaches that have targeted **CEA** include vaccination with recombinant **CEA** protein, **CEA** anti-idiotype antibodies, and dendritic cells pulsed with **agonist epitopes** of **CEA**. Humoral responses have predominantly been induced with the first two approaches, whereas CD4 and CD8 responses, disease stabilization, and even objective clinical responses have been seen with the dendritic cell approach. Recently, **CEA**-poxvirus vectors encoding **CEA** and costimulatory molecules such as B7.1 have been shown to be safe and to induce increases in the frequency of T-cell precursors that recognize processed **epitopes** of **CEA** presented on MHC class 1 molecules. Disease stabilization has been seen in up to 37% of patients treated with these vaccines. CONCLUSION: Tolerance to **CEA** in patients with cancer can be overcome with several different vaccination approaches, and such vaccinations are safe and immunologically active. Poxvirus-based vaccines can reproducibly generate T-cell responses to **CEA** and to tumors expressing **CEA**. Clinical activity has been seen with poxvirus or dendritic cell approaches. Other approaches are also being explored.

=> dis l14 ibib abs 2-3

L14 ANSWER 2 OF 3 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999172096 EMBASE
TITLE: Production and characterization of 22 monoclonal antibodies directed against S 20499, a new potent 5-HT(1A) chiral **agonist**: Influence of the hapten structure on specificity and stereorecognition.
AUTHOR: Got P.; Raimbaud E.; Bussey C.; Caron G.; Carrupt P.-A.; Walther B.; Bensussan A.; Scherrmann J.-M.
CORPORATE SOURCE: B. Walther, Technologie Servier, F-45000 Orleans, France
SOURCE: Pharmaceutical Research, (1999) 16/5 (725-735).
Refs: 30
ISSN: 0724-8741 CODEN: PHREEB
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Purpose. An immunoconjugate model was proposed to produce stereoselective monoclonal antibodies (MAbs) for the quantitation of a 5HT(1A) **agonist**, S 20499. MAbs produced were characterized in terms of stereoselectivity and specificity towards the opposite enantiomer and structural analogs. Methods. The immunogen was formed following the effective addition of a butanoic acid spacer arm between the parent S 20499 structure and bovine serum albumin (BSA). After fusion (modified Kohler and Milstein's procedure), specificity of MAbs was obtained using the Abraham's criteria. Experimental and calculated partition coefficients were determined. Results. Twenty-two hybridoma cell lines were established secreting MAbs (apparent association constants ranging from 1.1 x 108 to 2.8 x 109 M-1). Several MAbs showed cross-reactivity levels of less than 5% with S 20500 (optical antipode), which could allow a stereospecific assay to be set up. Both chroman and azaspiro moieties were part of the **epitopic** site. Dealkylation and hydroxylation(s) led to various crossreactivity levels. Four antibody families were described in terms of specificity. Conclusions. This study highlighted the influence of the immunoconjugate construction (coupling site and type of spacer arm) in the immuno-stereospecificity of Abs. The results obtained for two monohydroxylated metabolites suggest that the lipophilicity behavior could be a valuable tool for predicting Ab-crossreactivity.

L14 ANSWER 3 OF 3 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2000:230389 BIOSIS
DOCUMENT NUMBER: PREV200000230389
TITLE: Immunization with **CEA agonist epitope** pulsed Flt3L expanded dendritic cells for human tumor immunotherapy.
AUTHOR(S): Fong, Lawrence H. (1); Hou, Y. (1); Benlke, C. (1); Yuen, A. (1); Fisher, G. A. (1); Engleman, E. G. (1)
CORPORATE SOURCE: (1) Stanford Univ Sch of Medicine, Palo Alto, CA USA
SOURCE: Proceedings of the American Association for Cancer Research

Annual Meeting, (March, 2[redacted] No. 41, pp. 217-218.
Meeting Info.: 91st Annual Meeting of the American
Association for Cancer Research. San Francisco, California,
USA April 01-05, 2000
ISSN: 0197-016X.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English